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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RIGGS II, LARRY D	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,458	VITIELLO ET AL.	
	Examiner	Art Unit	
	LARRY D. RIGGS II	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed 08 July 2008 are acknowledged and entered.

Status of Claims

Cancellation of claims 1-26 and 32-44 are acknowledged. Claims 27-31 are currently pending and under consideration.

Withdrawn Rejections/Objections

The objection of the disclosure in the Office action mailed 08 April 2008 is withdrawn in view of the amendments filed 08 July 2008.

The objection to claims 27 in the Office action mailed 08 April 2008 is withdrawn in view of the amendments filed 08 July 2008.

The rejection of claims 27-31 under 35 U.S.C. 112, Second Paragraph in the Office action mailed 08 April 2008 is withdrawn in view of the amendments filed 08 July 2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27-31 rejected under 35 U.S.C. 103(a) as being unpatentable over Bellinger-Kawahara et al., (US 6,964,856) in view of Laudes et al., (Am. J. Pathology, 2002, 160(5), 1867-1875) and further in view of Anderson et al., (US Pat. Pub. 2003/0194752).

The instant claims 27-31 provide a method of evaluating a test compound for treating sepsis syndrome, comprising:

(a) developing experimental animals modeling sepsis syndrome, comprising infecting experimental immunocompromised animals and control immunocompromised

animals of the same species with a pathogen species capable of causing sepsis in the animal species, wherein the survival rate of the experimental immunocompromised infected is 10-90%;

(b) administering a test compound to the experimental animals;

(c) obtaining biological samples from the experimental and control animals at a selected timepoint following infection;

(d) measuring the amounts Of a plurality of analytes in the biological samples;

(e) determining the-scores for the biological samples from the experimental and control animals using a discrimination function for the animal species, wherein the discrimination function is 19(MCP-I-JE) + 27(IL-6) + 18(MCP-3) + 2 I(I.L-3) + 18(MIP-I [3) + 25(KC-GRO); and

(f) evaluating the test compound for suitability as a candidate drug for treating sepsis syndrome based on its effectiveness in causing a statistically significant change in the score for the biological samples from the experimental animals compared to the score for the biological samples from the control animals.

Regarding claims 27 and 31, Bellinger-Kawahara et al. shows a method of evaluating a test compound for treating sepsis by infecting experimental and control immunocompromised animals, with a pathogen capable of causing sepsis, wherein the survival rate of the infected animal was 39%, then administering the test drug to the experimental animals, a level of reporter in the experimental and control animals is measured at a select time interval after onset of sepsis, and selecting the test drug as a candidate drug for treating sepsis if the test drug is effective to cause a statistically-

significant reduction in the level of reporter in the experimental animals compared with the control animals, (see abstract; column 2, lines 51-67; column 8, lines 20-56; column 12, line 54 – column 13, line 10; column 17, line 40 – column 18, line 38; Table 3).

Bellinger-Kawahara et al. does not show (c) obtaining biological samples from the experimental and control animals of the same species, at a selected timepoint following infection; (d) measuring the amounts of a plurality of analytes in the biological samples; and part of step (e), determining the scores for the experimental and control animals using a discrimination function for the animal species.

Laudes et al. shows obtaining samples from experimental and control animals of the same species, (see page 1868, right column, paragraphs 2-3) and measured the amounts of analytes, such as APTT, PT, D-dimer, platelet counts and fibrinogen levels, etc., at selected time points of 12, 24 and 36 hours, (See figures 2-8). It would be obvious to monitor analytes associated with biological pathways affected during sepsis.

Bellinger-Kawahara et al. and Laudes et al. do not show determining scores for the experimental and control animals using a discrimination function.

The specification provides a definition of the discrimination function as "a linear function of measured variables", (page 17). Anderson et al. shows a discriminate model in which a score is computed for each patient, wherein the score is a linear function of the measured variables, and scores below a threshold are predicted to belong to on group and scores above the threshold are predicted to belong to another group, such as patients that progress to sepsis and patients that never progress to sepsis, (see paragraphs [0058], [0171]; Figure 1). Anderson et al. shows numerous linear functions

of measured variables, (paragraphs 155-170). It would be obvious to use linear functions associated with analytes that are monitored during Sepsis.

Regarding claims 28 and 30, Bellinger-Kawahara et al. shows that any test compound may encompass any compound or substance whose efficacy can be evaluated using the test animals and methods of the present invention, (see column 5, lines 4-15).

Regarding claim 29, Bellinger-Kawahara et al. shows 39% survival rate of immunocompromised infected animals, (see column 8, lines 20-56, column 17, line 40 – column 18, line 38; Table 3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of evaluating a test compound for treating sepsis by Bellinger-Kawahara et al. with the method of analysis and treatment of sepsis by Laudes et al. and the model of discriminate analysis and classification by Anderson et al. because the classification model, that enables prediction of patients entering sepsis, combined with the analysis of analytes during treatment of sepsis by Laudes et al., would allow accurate predictions with various linear functions relative to the evaluated analytes as in Anderson et al. to determine whether animals will likely suffer sepsis and effectively treat the sepsis, (see Bellinger-Kawahara et al., column 1, lines, 47-52).

Response to Arguments

Applicant's arguments filed 08 July 2008 have been fully considered but they are not persuasive.

Applicants argue that the amended claims the references fail to teach or suggest a method comprising the steps of developing experimental animals modeling Sepsis syndrome, administering a test compound to the experimental animals, obtaining biological samples from the experimental animals as well as from controls, measuring analytes in the biological samples, determining scores for the samples from the experimental animals and controls based on a discrimination function, and evaluating the test compound based on the comparative scores as recited in claim 27, wherein the discrimination function is 19(MCP- 1-JE) + 27(IL-6) + ! 8(MCP-3) + 21(IL-3) + 18(MIP-1~) + 25(KC-GRO) and evaluating the test compound based on the comparative scores as recited in claim 31,whereinthe analytes comprise Apolipoprotein A1, 1~2 Microglobulin, C Reactive Protein, D-dimer, EGF, Endothelin-1, Eotaxin, Factor VII, FGF-9, FGF-Basic, Fibrinogen, GCP-2, LIX, GM-CSF, Growth Hormone, GST, Haptoglobin, IFN-c, IgA, IL-10, IL-11, IL-12pT0, IL-17, IL-18, IE-lo~, IL-16, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7: Insulin IP-10, KC-GRO, Leptin, LIF, Lymphotactin,MCP-1-JE, MCP-3, MCP-5, M-CSF, MDC, MIP-lo~, MIP-11~, MIP-lot, MIP-2, MIP-31~, Myoglobin, OSM, RANTES, SCF, SGOT, TIMP-.1, Tissue Factor, TNF-o~, TPO, VCAM-1, VEGF, and VWF.

Applicants arguments are not persuasive.

Laudes et al. shows evaluating numerous amounts of analytes, such as APTT, PT, D-dimer, platelet counts and fibrinogen levels, etc., at selected time points of 12, 24 and 36 hours, (See figures 2-8). Anderson et al. shows decision rules based on a number of markers (analytes) to determine a threshold for whether patients enter

sepsis, (paragraph 170). It would be obvious to one skilled in the art to analyze numerous analytes during treatment of sepsis and use various linear functions relative to the evaluated analytes to determine whether animals will likely suffer sepsis and effectively treat the sepsis.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shubo (Joe) Zhou/
Primary Examiner, Art Unit 1631

/LDR/
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Examiner, Art Unit 1631